Two Separate Synchronous Primary Genitourinary Tumors

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A 54-year-old man presented to the office with gross painless hematuria, dysuria, and urinary frequency. He was diagnosed with renal cell carcinoma of the kidney and transitional cell carcinoma of the bladder. The article reviews the presentation, radiology, pathology, and intervention of an uncommon case of synchronous primary carcinomas, and aims to show the importance of continued clinical suspicion for multiple genitourinary primary neoplasms.

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KEY WORDS

Genitourinary tumor • Hematuria • Dysuria • Neoplasm • Urinary frequency

Multiple primary malignant neoplasms (MPMNs) were first characterized over 100 years ago. Over the course of the past century, our understanding of tumor biology, as well as our ability to expeditiously and efficiently diagnose malignancies, has improved immensely. Consequently, the diagnoses of MPMNs are still uncommon. Multiple studies, however, have shown that the genitourinary system may be particularly prone to multiple malignant neoplasm formation. In the United States, the incidence of genitourinary tumors is on the rise.[1] Over the past 5 years, the number of newly diagnosed genitourinary cancers has increased by approximately 10%.[2] It is reasonable to assume that as the number of tumors increases so will the diagnosis of MPMNs. There is little documentation of synchronous primary genitourinary malignancies being described in the United States. We present a case of a man with gross hematuria who was diagnosed with synchronous renal and bladder tumors.

Case Report

A 54-year-old man presented with painless gross hematuria, dysuria, and urinary frequency. The patient's past medical history is significant for

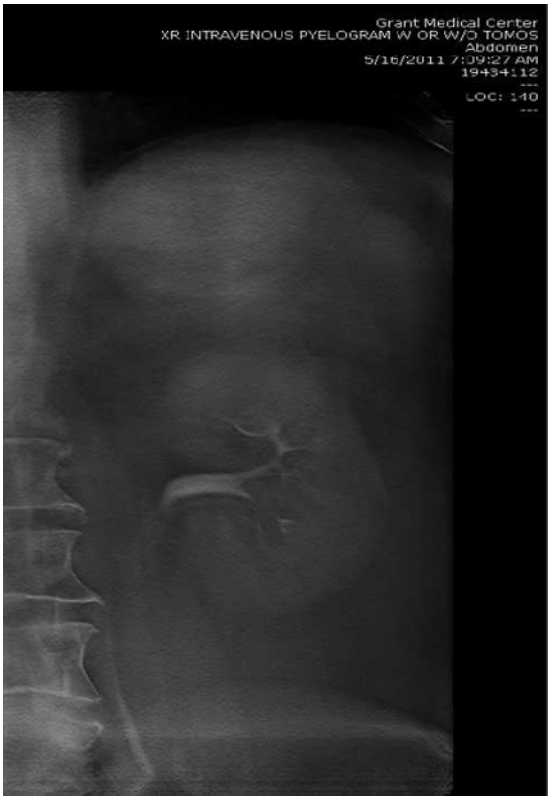

Figure 1. Intravenous pyelogram showing a left superior renal calyx deformity.

hypertension, benign prostatic hypertrophy, and non–insulin-dependent diabetes mellitus. Previous surgical history consists of an appendectomy, tonsillectomy, and adenoidectomy. He reported a 30-pack per year history of tobacco use; however, he stated he quit roughly 5 years prior to presentation. He drinks approximately 4 beers a day. Basic laboratory evaluations included a complete blood count and comprehensive metabolic panel, which demonstrated elevated aspartate aminotransferase and alanine aminotransferase. Urinalysis was significant for gross hematuria and pyuria. Radiologic evaluation consisted of an intravenous (IV) pyelogram, ultrasound, magnetic resonance imaging (MRI), and computed tomography.

An IV pyelographic study with tomography was significant for a mild deformity of the left superior renal calyx suggesting the possibility of an intrinsic renal mass (Figure 1). Evidence of mild prostatic enlargement was also noted. A follow-up ultrasound revealed a diffusely thickened bladder wall as well as a heterogeneous echogenic mass in the left upper pole of the kidney (Figure 2). To further characterize his mass, he received MRI of the kidney (Figure 3). This again demonstrated a left kidney mass measuring 5.5 × 4.5 × 5 cm in diameter without evidence of periaortic or pericaval adenopathy. Findings were consistent with a malignant neoplasm of the kidney.

Given the degree of uncertainty regarding histology and possible ureteral involvement, we proceeded with ureteroscopy with washing of the upper pole of the kidney to evaluate for transitional cell carcinoma. A 5-mL sample of cloudy pink fluid was obtained. Cytological analysis was negative for malignancy. The decision was then made to proceed with a left-hand-assisted laparoscopic radical nephrectomy. Histology confirmed a 5.7-cm clear cell renal cell carcinoma with a Fuhrman of grade 3 of 4 (Figure 4). The tumor was seen bulging into the renal sinus and compressing a small vein although no evidence of renal sinus fat infiltration or venous invasion was found. Margins were uninvolved. His pathologic stage is pT1bNxMx. His postoperative course was unremarkable and he was discharged home shortly after on Flomax® (tamsulosin hydrochloride; Boehringer Ingelheim Pharmaceuticals Incorporated, Ridgefield, CT) and Proscar® (finasteride; Merck and Co., Whitehouse Station, NJ).

Several weeks later he presented to the office with persistent urinary frequency, hesitancy, gross hematuria, and dysuria. Two weeks later, he underwent a cystoscopy and transurethral prostatic photovaporization with a GreenLight™ laser (American Medical Systems, Minnetonka, MN) for symptomatic benign prostatic hypertrophy.

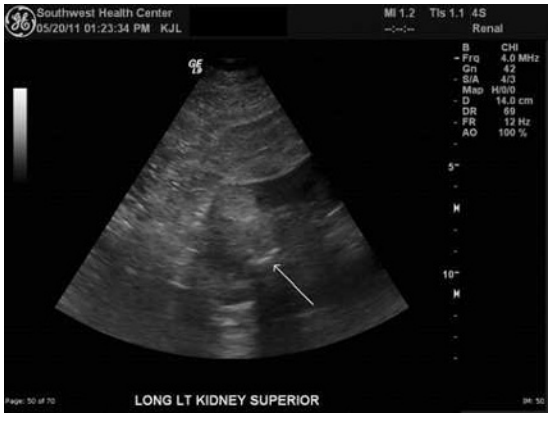

Figure 2. Ultrasound showing hyperechoic upper pole renal mass.

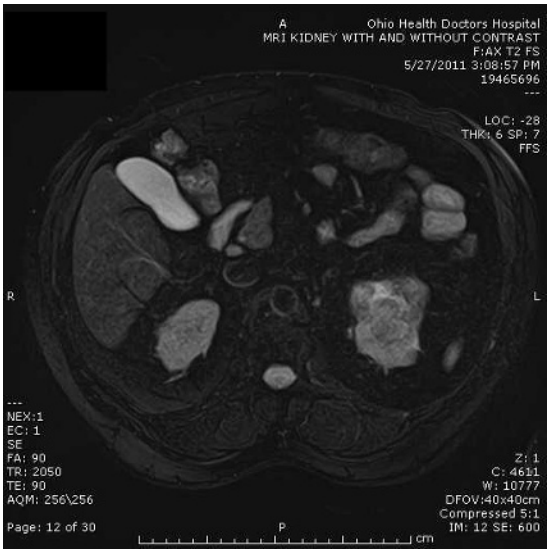

Figure 3. Magnetic resonance image showing a heterogeneous multilobular mass.

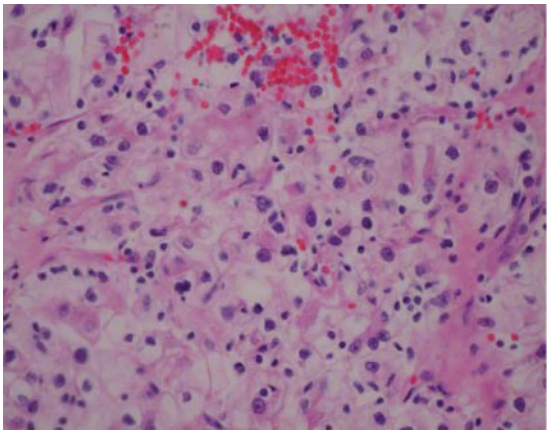

Figure 4. Histology confirming renal clear cell carcinoma. Large nuclei with prominent nucleoli. Fuhrman grade 3.

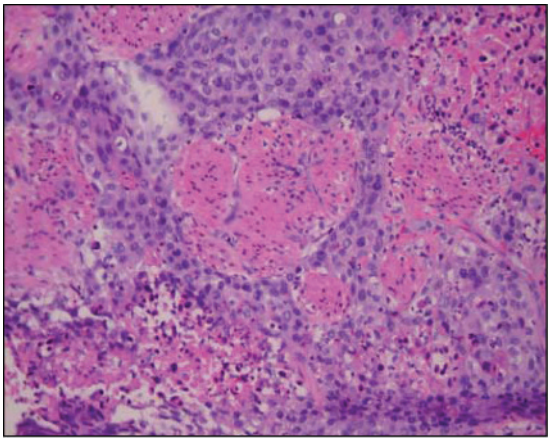

Figure 5. Histology confirming high-grade urothelial carcinoma invading around smooth muscle bundles.

Intraoperatively, he was noted to have what appeared to be a large sessile anterior bladder tumor approximately 4 cm posterior to the prostate. The lesion was not previously seen on cystoscopy. We abandoned the laser vaporization of the prostate and proceeded with a transurethral resection of the bladder tumor down to the bladder muscle fibers. Histology revealed a stage T2a high-grade papillary urothelial carcinoma with extensive invasion of smooth muscle (Figure 5). A CT scan of his chest, abdomen, and pelvis was obtained and was found to be negative for metastatic disease.

Given the invasive nature of his bladder cancer, we recommended neoadjuvant chemotherapy followed by a radical cystectomy with pelvic lymphadenectomy. He will undergo urinary diversion with a neobladder creation.

Discussion

In 1889, Theodore Bilroth was the first to describe multiple primary malignant neoplasms.[3] Approximately 40 years later, Warren and Gates developed criteria for diagnosing MPMNs: (1) each tumor must be malignant, (2) all neoplasms must be histologically distinct, and (3) metastatic link must be excluded.[4] In the United States, approximately 9% to 10% of all malignancies diagnosed are second primary tumors.[5] Multiple reports have suggested the genitourinary system to be increasingly susceptible to multiple primary malignant neoplasms.[6] The incidence of patients with urologic cancers having a second primary cancer has been reported to range from 2.8% to 6.3%.[7-9] Osman and colleagues reported that, following a urologic malignancy, the relative risk of a second primary neoplasm increased 1.11 times per month.[9] The literature proposes multiple theories for multiple primary tumor formation ranging from genetic, environmental, iatrogenic, and hormonal.

In the present case, we were able to successfully diagnose two separate primary malignancies involving both the kidney and the bladder. MPMNs of the genitourinary system are uncommon. In a review of the literature for simultaneous renal cell carcinoma and transitional cell carcinoma of the bladder, we found only 24 cases reported.[10-14] The majority of these cases occurred in Japan. Given the rising

incidence of synchronous malignancies, clinical suspicion is imperative for early diagnosis and successful management. ■

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MAIN POINTS

- The diagnosis of multiple primary malignant neoplasms (MPMNs) is uncommon. Studies have shown that the genitourinary system may be particularly prone to multiple malignant neoplasm formation, and in the United States, the incidence of genitourinary tumors is on the rise. In the past 5 years, the number of newly diagnosed genitourinary cancers has increased by approximately 10% and, as the number of tumors increases, so will the diagnosis of MPMN.
- Criteria for diagnosing MPMNs include the following: (1) each tumor must be malignant, (2) all neoplasms must be histologically distinct, and (3) metastatic link must be excluded.
- In the United States, approximately 9% to 10% of all malignancies diagnosed are second primary tumors. Reports suggest that the genitourinary system is increasingly susceptible to multiple primary malignant neoplasms, with the incidence reported to range from 2.8% to 6.3%.
- Given the rising incidence of synchronous malignancies, clinical suspicion is imperative for early diagnosis and successful management of MPMNs.